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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
FREDMAN, JEFFREY NORMAN	
ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 06/07/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/744,097	SHAFER, DAVID A	
	Examiner	Art Unit	
	Jeffrey Fredman	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 April 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *28,30-35 and 59-61* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28,30-35 and 59-61* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on April 28, 2006 has been entered.

Status

2. Claims 28, 30-35, 59-61 are pending.

Claims 28, 30-35, 59-61 are rejected.

Any rejection which is not reiterated in this action is hereby withdrawn as no longer applicable.

Election/Restrictions

3. Applicant requests that the sequence election be withdrawn because the invention will not work if the claims are limited to one nucleotide sequence. In this case, there are generic claims and specific claims drawn to SEQ ID NO: 76. The restriction requirement will currently be maintained. If a generic claim is ever found to be allowable, Applicant will be permitted to rejoin at least one additional sequence at that time. Until such time however, the restriction requirement is maintained and remains final.

Claim Interpretation

4. Applicant's amendment has significantly altered the claims. Claim 28 now describes a structure for the probe unit in which two probes are hybridized to one another with certain regions. The claim discusses a first and second universal probe linker, but is open to situations where these linkers are identical or different. The method continues to use the open transitional phrase "comprising". As MPEP 2111.03 notes "The transitional term "comprising", which is synonymous with "including," "containing," or "characterized by," is inclusive or open-ended and does not exclude additional, unrecited elements or method steps."

Arguably, the claim amendment is now drawn to a different invention than that originally claimed, but in view of the RCE, the amendment will be entered.

Claim Rejections - 35 USC § 112

5. Claims 28, 30-35, 59-61 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

As MPEP 2163.06 notes " If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. In re Rasmussen , 650 F.2d 1212, 211 USPQ 323 (CCPA 1981)."

Here, claim 28 incorporates apparently new matter. The new language "two oligonucleotides overlapped end to end to form a linear probe" lacks support in the

invention and is indefinite as discussed below. Similarly, the phrase "a first universal probe linker on one end that hybridizes to a universal reporter linker of a reporter by does not bind the single stranded target sequence" also lacks any basis in the specification. No basis was identified for the amendment by the Applicant in the response. A careful review by the examiner of the specification failed to identify any support for this new limitation.

Further with regard to the phrase "a first universal probe linker on one end that hybridizes to a universal reporter linker of a reporter by does not bind the single stranded target sequence", no support for the negative limitation of not binding target sequence is identified. As noted by MPEP 2173.05(I),

> " Any negative limitation or exclusionary proviso must have basis in the original disclosure. See Ex parte Grasselli , 231 USPQ 393 (Bd. App. 1983) aff'd mem., 738 F.2d 453 (Fed. Cir. 1984). The mere absence of a positive recitation is not basis for an exclusion. Any claim containing a negative limitation which does not have basis in the original disclosure should be rejected under 35 U.S.C. 112, first paragraph as failing to comply with the written description requirement."

Since no basis has been found to support the new claim limitations in the specification, the claims are rejected as incorporating new matter.

6. Claims 28, 30-35, 59-61 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is vague and indefinite what is meant by "two oligonucleotides overlapped end to end to form a linear probe". It is unclear if this means that the two oligonucleotides must simply be hybridized to one another, in which case that simpler language should

be used. It is indefinite whether the claim wants to require a complete overlap or a partial overlap, so only a partial overlap will be required for the prior art. Further "end to end" is unclear since it is indefinite if abutting or hybridizing or some other undefined interaction is intended. This wording is awkward, lacks apparent support in the specification and is vague and indefinite.

Claim 59 is indefinite since it depends from cancelled claim 29. For purposes of prior art, claim 59 will be treated as dependent upon claim 28.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 28 and 30-32, are rejected under 35 U.S.C. 102(b) as being anticipated by Wang et al (U.S. Patent 4,925,785).

Wang teaches a method for detecting a target nucleotide sequence (see abstract) comprising:

a) rendering the target nucleotide sequence substantially single stranded to give a single-stranded target nucleotide sequence (see column 3, lines 64-65 and figure 4C),

b) hybridizing the single stranded target nucleotide sequence with a nucleic acid probe unit (see figure 4C and example 2, columns 11 and 12) where two oligonucleotides are overlapped (hybridized, see figure 4C and column 12),

wherein the first oligonucleotide comprising three segments sequentially (see figure 16),

i) a first universal probe linker on one end that hybridizes to a universal reporter linker of a reporter by does not bind the single stranded target sequence (see in figure 4C and example 2, where the Pj probe has a region A, which is a universal linker that binds to the A' probe region and functions as the universal reporter linker and this region does not bind the single stranded target sequence)

ii) a central sequence complementary to the single stranded target sequence (see figure 4C and example 2, where there is a region of the Pj probe which is hybridizing to the single stranded target) and

iii) an overlap linker on the other end which can hybridize to the matching overlap linker of the second oligonucleotide (see the terminal region of the Pj probe, B, which hybridizes to the B' region of the second oligonucleotide),

wherein the second oligonucleotide comprises two segments sequentially,

i) a matching overlap linker that is hybridized to the overlap linker of the first oligonucleotide (see figure 4C, where second probe is hybridized to the Pj probe at the B region)

ii) a second universal probe linker which hybridizes to a universal reporter linker of a reporter but does not bind the single stranded target nucleotide sequence (see figure 4C where the sequence between B' and D' binds another probe but does not bind the target sequence),

c) washing to remove any unbound probe (see column 12, lines 11-12, for example which teach removal of the unhybridized complex),

d) hybridizing reporters to the two probe linker (see example 3 and figure 8, where labeled polymer is added for detection),

e) detecting the presence of said reporter to indicate the target sequence (see figure 4C, figure 8 and examples 1-3).

With regard to claim 30, Wang teaches the use of a double stranded reporter that is linked to a universal reporter linker (see figure 4C and column 6, lines 45-65, especially lines 60-61 "A probe can have one attached universal sequence to direct labelled hybridized nucleic acids to a particular location".

With regard to claim 31, Wang teaches probes that are up to 300 bases long (see column 12, lines 9-10).

With regard to claim 32, Wang teaches formation of a reporter array with multiple probes (see figure 6, for example).

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. Claims 33-35 and 59-60 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wang et al (U.S. Patent 4,925,785) in view of Urdea et al (U.S. Patent 5,681,697).

Wang teaches a method for detecting a target nucleotide sequence (see abstract) comprising:

a) rendering the target nucleotide sequence substantially single stranded to give a single-stranded target nucleotide sequence (see column 3, lines 64-65 and figure 4C),

b) hybridizing the single stranded target nucleotide sequence with a nucleic acid probe unit (see figure 4C and example 2, columns 11 and 12) where two oligonucleotides are overlapped (hybridized, see figure 4C and column 12),

wherein the first oligonucleotide comprising three segments sequentially (see figure 16),

i) a first universal probe linker on one end that hybridizes to a universal reporter linker of a reporter by does not bind the single stranded target sequence (see in figure 4C and example 2, where the Pj probe has a region A, which is a universal linker that binds to the A' probe region and functions as the universal reporter linker and this region does not bind the single stranded target sequence)

ii) a central sequence complementary to the single stranded target sequence (see figure 4C and example 2, where there is a region of the Pj probe which is hybridizing to the single stranded target) and

iii) an overlap linker on the other end which can hybridize to the matching overlap linker of the second oligonucleotide (see the terminal region of the Pj probe, B, which hybridizes to the B' region of the second oligonucleotide), wherein the second oligonucleotide comprises two segments sequentially,

i) a matching overlap linker that is hybridized to the overlap linker of the first oligonucleotide (see figure 4C, where second probe is hybridized to the Pj probe at the B region)

ii) a second universal probe linker which hybridizes to a universal reporter linker of a reporter but does not bind the single stranded target nucleotide sequence (see figure 4C where the sequence between B' and D' binds another probe but does not bind the target sequence),

c) washing to remove any unbound probe (see column 12, lines 11-12, for example which teach removal of the unhybridized complex),

d) hybridizing reporters to the two probe linker (see example 3 and figure 8, where labeled polymer is added for detection),

e) detecting the presence of said reporter to indicate the target sequence (see figure 4C, figure 8 and examples 1-3).

With regard to claim 30, Wang teaches the use of a double stranded reporter that is linked to a universal reporter linker (see figure 4C and column 6, lines 45-65, especially lines 60-61 "A probe can have one attached universal sequence to direct labelled hybridized nucleic acids to a particular location".

With regard to claim 31, Wang teaches probes that are up to 300 bases long (see column 12, lines 9-10).

With regard to claim 32, Wang teaches formation of a reporter array with multiple probes (see figure 6, for example).

Wang does not expressly teach the use of nucleic acid reporter arrays such as those of Urdea

Urdea teaches a method for detecting a target nucleotide sequence (see abstract) comprising:

a) rendering the target nucleotide sequence substantially single stranded to give a single-stranded target nucleotide sequence (see figure 1 and column 11, lines 37-39, where Urdea teaches the use of single stranded target sequence),

b) hybridizing the single stranded target nucleotide sequence with a nucleic acid probe (see figure 1 and column 11, lines 37-45) where the nucleic acid probe comprises a central sequence complementary to the target sequence and further comprises a probe linker at one terminal end which probe linker comprises a single stranded nucleotide sequence that does not hybridize to the target sequence (see figure 1 and column 10, line 61 to column 11, line 7, where the label extender probe comprises a region which hybridizes to the target and a second region which does not hybridize to the target),\

c) washing to remove any unbound probe (see figure 1 and column 11, lines 57-59),

d) joining the reporter to the linker (see figure 1 and column 11, lines 49-65),

e) detecting the presence of said reporter to indicate the target sequence (see figure 1 and column 11, line 65).

With regard to claim 30, Urdea teaches a probe which comprises a first and second terminal probe linker (see figure 16, where the LE has an X and Y region that hybridizes to the Amp1 probe).

With regard to claim 34, Urdea teaches a direct interaction between the reporter and terminal probe linker (see figure 1).

With regard to claims 31, 32, 33, 35, Urdea teaches a multi-linking unit (which is a reporter array) which is double stranded in the interaction with the LE probe which is interposed between the reporter linker and the terminal linkers, where the multilinking unit of figure 8, for example, comprises single stranded regions which hybridize with multiple reporter probes placed end to end which hybridize to the unit which is hybridized to the terminal linkers and where there is a "terminator" or terminal reporter probe (see figures 1, 8 and 16).

With regard to claim 59, many of the Urdea probes comprise a TA sequence including, SEQ ID NO: 35 (see column 23, line 27, for example).

With regard to claim 60, Urdea teaches spacer segments which will comprise carbon (see column 8, lines 10-37, for example).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to utilize the reporter system of Urdea as the signal amplification method in the method of Wang since Urdea teaches "The invention increases both the sensitivity and specificity of such assays, by reducing the incidence of signal generation that occurs in the absence of target, and does not involve a substantial increase in either time or cost relative to current assay configurations. In certain embodiments, the invention is also effective in compensating for the loss in signal that can result when background noise is reduced. (see column 2, lines 45-51)." An ordinary practitioner, motivated by Wang to improve signal (see column 6, lines 1-40, for example), would have been motivated to use the signal amplification method of Urdea since it would improve sensitivity, specificity and compensate for signal reduction.

Response to Arguments

11. Applicant's arguments with respect to the claims have been considered but are moot in view of the new ground(s) of rejection necessitated by Applicant's amendment.

Conclusion

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey Fredman whose telephone number is (571)272-0742. The examiner can normally be reached on 6:30-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571)272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Jeffrey Fredman
Primary Examiner
Art Unit 1637

v 6/6/01